REMARKS

Applicants have the following comments in support of this amendment and in response to the Office Action.

Claim Amendments – Reference to Disclosure

The claimed pharmaceutical compositions of the present application are directed to formulations of certain novel highly-halogenated halogenated xanthenes, including 4,5,6,7-Tetrabromoerythrosin, that are adapted for chemotherapeutic use. The specification of the present application makes it clear that such halogenated xanthenes may be in either a non-derivative or a derivative form, as is clear from the following passage:

> "[0023] The present invention is directed to new chemotherapeutic medicaments ... wherein a primary active component of such medicaments is a *halogenated xanthene or halogenated xanthene derivative*." Page 5 (emphasis added).

The identity of these forms is determined by the composition of the functionalities at positions R^1 and R^2, as illustrated by the following from the present application:

> "[0027] Selected chemical and physical properties (such as chemical constituents at positions X, Y, and Z and functionalities R^1 and R^2) of representative halogenated xanthenes are summarized in attached Table 1." Page 7.

Table 1 shows representative examples of these functionalities, including hydrogen atoms (i.e., if R^1 and R^2 are both hydrogen atoms, the halogenated xanthene is in its acid form), various monovalent cations (i.e., such as Na+, K+, and Li+, the last cation being disclosed in Table 1 of USSN 09/635,276 of which the present application is a continuation-in-part and which is incorporated by reference in the present application), and various organic constituents (i.e., an ethyl

group, as per the example of ethyl eosin). Applicants note that when these molecules are at physiologic pH (i.e., 5-7), they are in the dibasic form (i.e., both hydrogen atoms at R^1 and R^2 are replaced with monovalent cations, as for instance in the listed examples of disodium rose bengal and disodium 4,5,6,7-tetrabromoerythrosin).

The aforementioned acid forms of the halogenated xanthenes, along with the example dibasic forms, constitute non-derivative forms of these molecules, while the forms having organic constituents at R^1 or R^2 are derivative forms. This standard nomenclature is further illustrated by the following passage from the present application:

> "[0045] Moreover, that the facility with which the halogenated xanthenes target specific tissues or other sites can be further optimized by *attachment of specific functional derivatives* at positions R^1 and R^2.... An example of this is esterification at position R^1 with a short aliphatic alcohol, such as n-hexanol, to produce a *derivatized agent* exhibiting enhanced partitioning into lipid-rich tumor tissues.
> "[0046] It is thus a further preferred embodiment that at least one of the at least one *halogenated xanthene active ingredients includes at least one targeting moiety* selected from a group that includes DNA, RNA, amino acids, proteins, *antibodies*, ligands, haptens, carbohydrate receptors or complexing agents, lipid receptors or complexing agents, protein receptors or complexing agents, chelators, encapsulating vehicles, short- or long-chain aliphatic or aromatic hydrocarbons, including those containing aldehydes, ketones, alcohols, esters, amides, amines, nitriles, azides, or other hydrophilic or hydrophobic moieties. A further example of this embodiment is derivatization of Rose Bengal with a lipid (at position R^1, via esterification), so as to increase the lipophilicity of Rose Bengal, and thereby modify its targeting properties in a patient...." Pages 13-14 (emphasis added).

This makes it clear that ethyl eosin (of Table1) is a derivative form of eosin. The passage also lists a range of example organic constituents that, if attached to position R^1 or R^2, render the halogenated

xanthene a *halogenated xanthene derivative* (i.e., containing a functional derivative at position R^1 or R^2).

Therefore, it is clear that the present application discloses both non-derivative and derivative halogenated xanthenes in the present invention. Applicants are amending independent Claims 1 and 19 to be directed to the embodiment of the present invention consisting of non-halogenated xanthenes. Specifically, by claiming only those halogenated xanthenes that do not contain a functional derivative at position R^1 or R^2, it is clear that the presently claimed invention does not encompass halogenated xanthenes that contain organic constituents at positions R^1 or R^2 but rather are directed to pharmaceutical compositions consisting of non-derivative halogenated xanthenes.

Accordingly, Applicants respectfully submit that the amendments to Claims 1 and 19 are not adding any new matter and are clearly supported by the application as filed. Therefore, it is requested that they be entered.

Finally, in order to advance the prosecution of this application Applicants have canceled Claim 20 without prejudice or disclaimer.

Novel Composition of Matter

As Applicants noted in Amendment E, filed on May 23, 2005, amended independent Claims 1 and 19 are directed to various pharmaceutical compositions that contain certain highly-halogenated halogenated xanthenes, including 4,5,6,7-Tetrabromoerythrosin, none of which are believed to have been described in the prior art. Due to the relative complexity of synthesis of such compounds and other factors, such as stability considerations, Applicants believe they have invented new compounds which represent a novel extension to the halogenated xanthene family. Accordingly, Applicants

respectfully submit that the claimed highly-halogenated halogenated xanthenes and the various claimed pharmaceutical compositions containing such highly-halogenated halogenated xanthenes of the claims of the present application are novel over the prior art.

Applicants will now address each of the Examiner's comments and rejections in the order in which they appear in the Office Action.

Priority

In the Office Action, the Examiner objects to the priority statement on page 1 of the specification for informalities therein.

Accordingly, Applicants are amending paragraph [0001] of the specification to correct certain alleged informalities in the language concerning the claimed priority. In particular, Applicants are adopting the Examiner's suggested language with regard to provisional application '464. In addition, Applicants are amending the specification to state that the present non-provisional application is a continuation-in-part of the '041, '276 and '785 non-provisional applications. It is believed that this overcomes each of the Examiner's objections to the priority statement in the specification.

Further, this paragraph is being amended to recite that the '276 application is a continuation-in-part of US application 09/216,787 filed December 21, 1998. When originally filed, the present application was designated at a continuation-in-part of US application 09/635,276, which itself was already designation as a continuation-in-part of US application 09/216,787 (along with other applications). The '785 application has a similar designation (along with designation other

applications; the '041 application also designates another application). This amendment to paragraph 1 clarifies the relationship of the present application to the 10/216,787 application.

Claim Rejections – 35 USC §102

The Examiner also rejects Claims 1, 9-11, 19 and 27 under 35 U.S.C. §102(e) as being anticipated by Dees et al. (US 6,331,286). This rejection is respectfully traversed for at least the following reasons.

In particular, the present application is a continuation-in-part of US application '276 which is a continuation-in-part of US application 09/216,787 (which became the Dees '286 patent). Hence, the present application claims priority back to Dees '286, and Dees '286 is not prior art to the present application.

Furthermore, whereas the radiosensitization methods of Dees are predicated on activation of a radiosensitizer (containing a halogenated xanthene) using applied ionizing radiation, the pharmaceutical compositions of the claimed invention avoids the necessity of applying radiation. Instead, the claimed invention is directed to novel pharmaceutical compositions which are pharmacologically active against cancer and other diseased tissues without the necessity of additional activation. Such directly chemotherapeutic compositions have improved utility over the teachings in Dees as it is preferable to treat cancer and other diseased tissue with only one substance, i.e. the claimed compositions, than having to add additional activating energy, such as the ionizing radiation of Dees, to the body.

Finally, with respect to independent Claim 19, Dees does not disclose delivery of a medicinal composition formulated in a delivery vehicle consisting of a tablet, a capsule, or a suppository.

Accordingly, for at least the above-stated reasons, Applicants respectfully request that this rejection be withdrawn.

Claim Rejections – 35 USC §112

The Examiner also rejects Claims 1-2, 9-11, 19-20 and 27 under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the written description requirement. This rejection is also respectfully traversed.

While Applicants traverse this rejection and still believe that there is support for the objected to language, in order to advance the prosecution of this application Applicants have amended independent Claims 1 and 19, removing reference to disodium or dipotassium salts.[1] Applicants have also canceled Claim 20 without prejudice or disclaimer. Applicants believe that such actions overcome the Examiner's stated reasons for the rejection of the subject claims under 35 U.S.C. §112, first paragraph.

Accordingly, it is respectfully requested that this rejection be withdrawn.

Interview Request

If the Examiner still wishes to reject the claims of the present application after considering this amendment, then Applicants request an interview with the Examiner to discuss the rejections

[1] While Applicants are amending the claims to remove the language regarding disodium or dipotassium salt, independent Claims 1 and 19 are still patentable over Goers, Bottiroli and Schultz as explained in prior Amendment E as none of these references disclose or suggest the claimed pharmaceutical compositions that contain certain highly halogentated xanthenes such as 4,5,6,7-Tetrabromoerythrosin, nor do any of these references disclose or suggest the claimed pharmaceutical compositions that contain non-derivative halogenated xanthenes.

in further depth. Therefore, in order to advance the prosecution of this application, it is respectfully requested that the Examiner please contact the undersigned to set-up such an interview prior to the issuance of a further Office Action for this application.

Conclusion

For at least the above-stated reasons, it is respectfully submitted that the claims of the present application are in an allowable form and are patentable over the cited references. Accordingly, it is requested that the application now be allowed.

If any fee should be due for this amendment, please charge our deposit account 50/1039.

Favorable reconsideration is earnestly solicited.

Respectfully submitted,

Date: November 18, 2005

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